



News release for medical media and national newspapers

NICE Recommends Xarelto[®] (rivaroxaban) use in NHS

The National Institute for Health and Clinical Excellence (NICE) has issued an initial positive opinion on the new oral anticoagulant Xarelto[®] for the prevention of potentially fatal blood clots after elective hip or knee replacement surgery. The Scottish Medicines Consortium (SMC) has already accepted rivaroxaban for use in NHS Scotland

London, 5th March 2009 – Bayer Schering Pharma welcome NICE's Final Appraisal Determination (FAD) giving a draft recommendation that Xarelto (rivaroxaban), within its marketing authorisation, is recommended as an option for the prevention of venous thromboembolism in adults having elective total hip or elective total knee replacement surgery. Xarelto is the first of a new generation of anticoagulants – oral direct Factor Xa inhibitors – and is the first oral anticoagulant to demonstrate superior efficacy to the current standard of care, injectable enoxaparin, whilst maintaining a comparable side effect profile.³

Venous thromboembolism (VTE) is a major patient safety issue, causing 10 per cent of all in-hospital deaths in the UK – 25,000 to 32,000 people each year – more than HIV/AIDS, breast cancer, and road traffic accidents combined.⁴ This makes VTE one of the leading causes of preventable hospital deaths in the UK. Major orthopaedic surgery is associated with a particularly high risk of hospital-acquired VTE due to the invasive nature of the procedure and the reduced mobility it causes. As a result up to half of the 90,434 people undergoing hip or knee replacement every year in England¹ could go on to develop a potentially fatal blood clot if no preventative treatment (known as thromboprophylaxis) were given.²

Professor Beverley Hunt, Consultant Haematologist and Medical Director of Lifeblood: The Thrombosis Charity, welcomes NICE's draft decision: "It is terrific that NICE have reviewed Xarelto[®] so quickly. A new highly effective oral anticoagulant will encourage the

thromboprophylaxis implementation and greatly reduce the risk of hospital-acquired clots after planned major orthopaedic surgery.”

In a large-scale Phase III clinical trial programme involving over 12,500 patients, rivaroxaban became the first oral anticoagulant to demonstrate superior efficacy over the current standard of care (injected enoxaparin). In these trials, rivaroxaban reduced the combined total of VTEs and deaths by between 49–79%.^{5,6,7} In addition to these efficacy advantages, rivaroxaban has other benefits compared with currently available treatment options because it is given as a one tablet, once-daily, fixed-dose regimen that eliminates the need for any routine monitoring (such as coagulation (clotting), liver function etc) or dose adjustment.⁸

Professor Ajay Kakkar, Professor of Surgical Sciences at the Barts and the London School of Medicine and Dentistry, and Director of the Thrombosis Research Institute, London said, “NICE’s provisional recommendation about rivaroxaban is very encouraging. Venous thromboembolism is the commonest avoidable cause of hospital death. Today’s announcement means we have another effective method to prevent potentially fatal blood clots in orthopaedic surgical patients. In particular we can now facilitate the use of preventative methods out of hospital.”

VTE costs the NHS an estimated £640 million per year.⁴ A further £19 million of NHS money is spent on litigation from patients who have developed blood clots as a result of a hospital stay or procedure.⁹

In line with normal NICE processes, the NICE recommendation is subject to appeal and correction of factual errors, with final NICE guidance expected in April. Xarelto[®] was licensed in the UK in October 2008 and received a positive SMC ruling in December 2008.

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CONTACT FOR FURTHER INFORMATION:

Athena Medical PR

Rawaa Abdalla
Tel: 020 8956 2870
Mobile: 07853 349 792
rawaa@athenamedicalpr.com

Emma Keeling
Tel: 020 8956 2294
Mobile: 07884 311982
emmak@athenamedicalpr.com

NOTES FOR EDITORS

National Institute for Health and Clinical Excellence recommendation*:

Rivaroxaban (Xarelto®), within its marketing authorisation, is recommended as an option for the prevention of venous thromboembolism in adults having elective total hip replacement surgery or elective total knee replacement surgery.

<http://www.nice.org.uk/guidance/index.jsp?action=download&o=43417>

About hospital-acquired DVT

- Venous blood clots, (also known as venous thromboembolism or VTE) can take the form of either:
 - A deep vein thrombosis (DVT) - a blood clot in a deep vein (usually in the leg) that partially or totally blocks the flow of blood¹⁰
 - A pulmonary embolism (PE) - a blood clot blocking an artery in the lungs¹⁰
- Each year an estimated 25,000 to 32,000 people in the UK die from venous blood clots as a result of a hospital stay or surgical procedure (sometimes referred to as 'hospital-acquired DVT'). This is more people than die from breast cancer, HIV/AIDS and road traffic accidents combined⁴
- Many of these deaths could be prevented⁴
- Effective prevention and treatment of hospital-acquired DVT is a major national public health issue⁴
- People at risk of hospital-acquired DVT include people undergoing major orthopaedic surgery and those who are hospitalised or immobilised over long periods^{11,12}
- The majority (74%) of hospital-acquired DVT cause symptoms after the patient has left hospital¹²
- Hospital-acquired DVT occur in up to 50% of patients undergoing major orthopaedic surgery who do not receive preventative care²
- In November 2008, the All-Party Parliamentary Thrombosis Group (APPTG) published their second annual report which showed that 70% of acute hospital trusts are now taking steps to risk assess patients for hospital-acquired DVT¹³ – compared with only 32% in their 2007 report.¹⁴ These findings demonstrate that more hospitals are now bringing their practices in line with NICE and government recommendations, which are as follows:
 - Current NICE recommendations state that:¹⁵
 - All patients undergoing major surgery should be assessed to identify their individual risk of developing VTE after the procedure

* Subject to appeal and correction of factual errors

- All patients undergoing major orthopaedic surgery of the lower limbs should receive anticoagulant therapy, LMWH (low molecular weight heparin) for up to 28 days after surgery in combination with pressure stockings, to reduce the risk of VTE
- SIGN guidelines recommend patients undergoing total hip or knee replacement surgery should be considered for both pharmaceutical thromboprophylaxis for up to five weeks following surgery, and mechanical methods of thromboprophylaxis¹⁶

About Xarelto® (rivaroxaban)

Xarelto® is licensed for the prevention of venous thromboembolism in adult patients undergoing elective hip or knee replacement surgery. It is the first of a new class of oral anticoagulant specifically inhibiting Factor Xa, a pivotal step in the coagulation (blood clotting) process.¹⁷

Unlike low molecular weight heparins, such as enoxaparin, which are administered daily by injection, Xarelto® is an oral, one tablet once-daily treatment which is administered six to ten hours after surgery.¹⁸ It is licensed for two weeks following elective knee replacement surgery or five weeks following elective hip replacement surgery. An oral tablet such as Xarelto® offers a more convenient, patient orientated treatment option than an injection as it enables patients to more easily continue their anticoagulant therapy at home, providing ongoing protection against the continued risk of developing clots. Further, there are no routine coagulation monitoring requirements with Xarelto®.

More than 60,000 patients are expected to be enrolled into the Xarelto clinical development program, which will evaluate the product in the prevention and treatment of a broad range of acute and chronic blood-clotting disorders.

About Bayer Schering Pharma UK

Bayer Schering Pharma is a leading, worldwide speciality pharmaceutical company. Its research and business activities are focussed on the fields of haematology & cardiology, oncology, diagnostic imaging, primary care, specialised therapeutics and women's healthcare. With innovative products and using new ideas, Bayer Schering Pharma aims to make a contribution to medical progress and strives to improve the quality of life of patients.

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